Genetic Maps → used exclusively as Starting point in Sequence of whole genome ← as in HUMAN GENOME PROJECT

POLYGENIC INHERITANCE

Many traits not so distinct & spread across a gradient.
Such traits controlled by 3 or more genes.

Besides involvement of multiple genes, polygenic inheritance takes into account influence of environment

Human Skin colour ← polygenic inheritance

In a polygenic trait, phenotype reflects the contribution of each allele i.e effect of each allele additive

All dominant (AABBCC) → Darkest } All recessive (aabbcc) → Lightest

3 dominant allele + 3 recessive allele → intermediate skin colour.

- No. of each type of alleles in genotype determines darkness/lightness of individual's skin

PLEIOTROPY

✱ Single gene → can exhibit multiple phenotypic expression → Pleiotropic gene

- Underlying Mechanism of pleiotropy in most cases → effect of a gene on metabolic pathways which contribute towards different phenotypes

- Ex → Phenylketonuria (single gene mutation) in humans → due to mutation in genes that codes for enzyme Phenylalanine hydroxylase

- Through Phenotypic expression characterised by: Mental Retard. | Reduction in hair | Skin pigment reduction

Phenylalanine hydroxylase manifests itself

SEX DETERMINATION

✱ Experiments on - Insects → cytological observations → led to concept of genetic/chromosomal basis of XXX determination

✱ Henking (1981) → noticed → specific nuclear str. all through spermatogenesis in a few insects → 50% of gamete received it, & 50% did not (sperm.me)

could not explain X-body significance.

X - body ← gave name

actually a chromosome

X - chromosome

Sex chromosome

In insects.
XO type → XX - females
XO - males.

XO → Males - have only 1 X chromosome besides autosomes
↳ Females - have a pair of X chromosome " "

Among males, X chr. - present → Y chr. = smaller.
its counterpart

either with or without X chr.

In both cases XY, XO type, males produce → some with X, some with Y

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Male heterogamety

Some insects

Birds → Female heterogamety
- Male - ZZ (Bigger tail)
- Female - ZW (Smaller tail)

Human Males & Females / Drosphila: Male XY, Female XX

Grasshopper: Males XO, Females XX

SEX DETERMINATION IN HUMANS

23 pairs chr. → 22 pair autosome, 1 pair sex chromosomes

♀ XX always → X ⇒ XX - Female

♂ X / Y — 50% chance of sperms be → X ⇒ XY - Male

Humans - XY determination of sex

Genetic make up of sperm decides → Sex of child.

Each pregnancy — 50% chance of either a male/female child.

SEX DETERMINATION IN HONEY BEE

Sex determination of honey bee based on → No of sets of chromosome an individual recieves.

egg + sperm → fertilized egg → develop as → female (queen, workers)

Females - Diploid - 32 chromosomes

Unfertilized egg develop as males/drone By ↓ parthenogenesis

Males - haploid - 16 chromosomes

Haplo-diploid sex determination system & has special charact. feature:

Males → prod. sperm by → Mitosis

They dont have father & thus cannot have sons but have grandfather & can have grandsons.

MUTATION

Mutations — results in alteration of DNA sequences & consequently results in change in → genotype, phenotype } of org.

Mutation, Recombination → Both causes variation in DNA.

DNA helix → runs continuously → from one end to other → in → Each chromatid (in highly supercoiled form)

Alteration of chr → results in → Abnormalities/aberration ← since genes located on chr. ← Alteration result in chromosome ← in ← of a segment end of DNA ← Loss (deletion), Gain (insertion, duplication) ← Therefore

(* Chromosomal abberations common in cancer cells (easily observed))

Deletion, Insertion → of bp of DNA causes → Frameshift mutation.

Mutation → arise due to → change in single bp of DNA → Point Mutation

Classic example — Sickle cell anaemia

Chemical, Physical → factors (referred to as mutagens) → induce → mutation

Example → UV rays — can cause mutation

GENETIC DISORDERS

- **Pedigree Analysis** → After rediscovery of Mendel's work → The practise of analysing inheritance pattern of traits in human being began.

Control crosses → pea plant ✓ | Human beings ✗ → hence → Study of family history about inheritance of particular trait provides an alternative.

In pedigree analysis, the inheritance of a particular trait is represented in family tree over generations.

Analysis of traits in several generations of a family.

Pedigree analysis

pedigree analysis provides → strong tool in human genetics

utilised to → trace the inheritance of → Specific trait | Abnormality | Disease

- Male
- female
- Sex unspecified
- Affected individuals
- 5 unaffected individuals
- mating
- consanguineous mating (mating b/w relatives)

DNA → transmitted from generation to generation without any change/alteration

However, change or alteration occur occasionly

Each & Every feature in organism → Controlled by → one or the other gene → located on → DNA → present on → Chromosome

DNA → carrier of genetic inf.

Many disorders in human beings have been found to be associated with inheritance of → MUTATION

MENDELIAN DISORDERS

Genetic Disorder → Mendelian disorder | Chromosomal disorder

Determined by → "Alteration / Mutation in the single gene"

These disorders are transmitted to offspring on → Some lines above we have studied in principle of inheritance

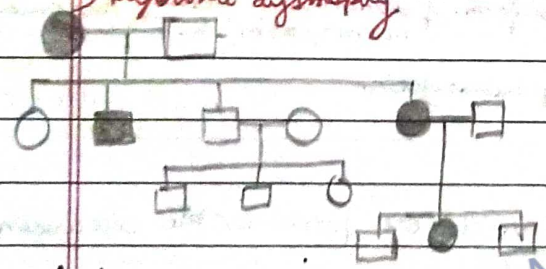
MENDELIAN DISORDERS may be → dominant / Recessive / Sex linked

- Haemophilia
- Cystic fibrosis
- Sickle cell anaemia
- Colour blindness
- Phenylketonuria.
- ~~Myotonic dystrophy~~

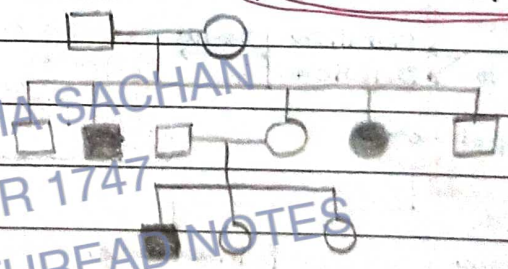
By pedigree analysis we can find out

Ex. → haemophilia (X-linked recessive) → Transmission from carrier female to male progeny

traced by pedigree analysis in a family. ← pattern of inheritance of these disorders



Autosomal dominant
– Myotonic Dystrophy



Autosomal recessive
– Sickle cell anaemia

(1) Colour Blindness – Sex-linked recessive → due to → defect in either red or green cone of eye

Males – 8%
Females – 0.4%

Mutation in certain genes present on X chromosome ← this defect is due to

Failure to discriminate b/w red & green colours. ← Resulting in

Males more → bcz genes that lead to red green colour blindness are on X chromosome. & males have only one X while women have 2 X.

(2) Haemophilia – Sex linked recessive transmission → some of male progeny unaffected carrier female

due to → single protein that is a part of the cascade of proteins involved in the clotting of blood is affected. → hence A simple cut will result in non stop bleeding.

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Mother – carrier

Father – haemophilic (invisible in many later stage of life)

- Possibility of female to be haemophilic extremely rare bcz for that
- Queen victoria's Pedigree shows no of haemophilic descendants & → carrier of disease

(3) Sickle Cell Anaemia – Autosomal recessive disease transmitted when Both parents heterozygous

Disease controlled by → A single pair of allele → Hb^A / Hb^S

$Hb^S Hb^S$ – diseased

$Hb^S Hb^A$ – carrier unaffected (50% possibility of transmitting mutant gene to the progeny)

Three genotypes possible → $Hb^A Hb^A$ / $Hb^A Hb^S$ / $Hb^S Hb^S$

Caused by – Substitution of Glutamic acid (Glu) by Valine (Val) at 6th position of β globin chain.

GAG to GUG ← single base mutation

Mutant Haemoglobin molecule – polymerise under low oxygen tension causing change in shape from biconcave → elongated sickle.

	Template		
Normal Hb(A) gene	-GAG-	Hb^S gene	GTG
coding	-CTC-		-CAC-
mRNA	GAG		GUG
	Glu		Val.

(Micrograph of RBCs)

(3) PHENYLKETONURIA – inborn error of metabolism → autosomal recessive

Affected individual — lacks enzyme that converts tyrosine → AA – phenylalanine → accumulated as phenylpyruvic acid & other derivatives

Accumulation is also excreted through urine bcz of its poor absorption by Kidney

Mental Retardation ← causes (accumulation in brain)

(4) THALASSEMIA: Autosomal-linked recessive → Transmitted when both parents heterozygous.

defect due to → Mutation / Deletion → results in → Reduced rate of synthesis of one the globin chains (α – β chains) → causes form. of abnormal haemoglobin → results in → Anaemia (characteristics of this disease)

→ make up haemoglobin

classified acc to which chain of haemog. mol. affected.

α-Thalassemia

- Prod. of α globin chain affected
- Controlled by 2 closely linked genes → HBA1 / HBA2 on chromo. 16 of each parent.
- Observed – due to deletion or mutation of one or more of 4 genes

β-Thalassemia

- Prod. of β-globin chain affected.
- Controlled by – single gene HBB on chr. 11 of each parent.
- Occurs due to – mutation of one or both the genes

Thalassemia differs from sickle cell anaemia

quantitative → Synthesising too few/few molecules of globin.

qualitative → synthesising an incorrectly functioning globin

CHROMOSOMAL DISORDER

caused due to → 'absence' or 'excess' or 'abnormal arrangement' of 1 or more chromosomes

* Aneuploidy → Gain / Loss of chromosome(s)
  due to → Failure of segregation of chromatids during cell division cycle.

* **Down's Syndrome** → gain of extra copy of chromosome 21.

Turner syndrome → Loss of an 'X-chr.' in human females.

Polyploidy → Failure of cytokinesis after telophase results in ↑ of whole set of chrom
→ Often, seen in PLANTS

* Total no. of chromosomes in normal human cell → 46 (23 pairs)
  - 22 pairs → autosome
  - 1 pair → sex chromosome

* Sometimes, an additional copy of chromosome may be
  - included in an individual → TRISOMY of a chromosome
  - lacking in any individual → MONOSOMY of a chromosome

DOWN'S SYNDROME

due to → presence of additional copy of chrom. 21
→ Trisomy of 21
first described by → Langdon down in → 1866

- Short statured
- Small Round head
- Furrowed tongue
- Partially open mouth
- Broad palm with characteristic palm crease
- Physical, Psychomotor, Mental development retarded.

KLINEFELTER'S SYNDROME

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due to → additional copy of X-chromosome

↓ resulting in

Karyotype of 47, XXY

Such individual has

- sterile
- overall masculine development
- Feminine characteristics → Gynaecomastia → development of breast.

TURNER'S SYNDROME

due to → absence of 1 X - chrom.

↓ resulting in

Karyotype of 45, XO

Such females are

- sterile
- Rudimentary ovaries
- Lack of other secondary sexual characters.